39. (Amended) A modified nucleotide sequence encoding a DNA polymerase which has an amino acid sequence that shares not less than 95% homology to a DNA polymerase isolated from a strain of *Bacillus stearothermophilus* or *Bacillus caldotenax*, having an amino acid sequence that shares not less than 95% homology to SEQ ID NO:4, which nucleotide sequence encodes threonine, proline and leucine residues at positions 342-344, respectively, and a tyrosine residue at position 422, wherein the DNA polymerase in its unmodified state has leucine, glutamate, and glutamate residues at positions 342-344, respectively, and a phenylalanine at position 422, the positions being determined based on a last lysine residue in the end of the sequence counted as position 588.

40. (Amended) The modified nucleotide sequence according to claim 39 which has the nucleotide sequence of SEQ ID NO:3.

REMARKS

Reconsideration and allowance of the subject application are respectfully requested.

The specification is amended above to correct the informalities regarding priority pointed out by the Examiner in the Office Action dated February 11, 2003. Claims 9, 29, 39 and 40 are amended above to address the Examiner's concerns regarding informalities and 35 U.S.C. §112, first and second paragraphs. None of the amendments to these claims introduces new matter, and some of the amendments are made to clarify the invention or to correct grammar. The amendatory language in independent claims 9, 29 and 39 regarding the DNA polymerase "having an amino acid sequence that shares not less than 95% homology to SEQ ID NO:4", and "wherein the DNA polymerase in its unmodified state has leucine, glutamate, and glutamate residues at positions 342-344, respectively, and a phenylalanine at position 422, the positions being determined based on a last lysine residue in the end of the sequence counted as position 588" is supported by the original specification, for instance at page 19, line 11 – page 20, line 6; page 26, line 16 – page 27, line 8; the sequence listing; the original claims 11, 16, 22 and 24; and

the Examples. With entry of this amendment, claims 9-13, 29, 30, 39 and 40 are pending. Entry and consideration of the amended specification and claims are requested.

In the Office Action, claims 9-13, 29- 30 and 39 were rejected as indefinite under 35 U.S.C. §112, second paragraph. For claims 29, 30 and 39, the Examiner deemed unclear the language "a DNA polymerase isolated from a strain of *Bacillus stearothermophilus* or *Bacillus caldotenax*", and the numbering scheme for reference to positions 342-344 and 422. The *Bacillus stearothermophilus* and *Bacillus caldotenax* strains are of course mesophilic bacteria. All DNA polymerases falling within the scope of these claims are derived from mesophilic bacteria and—as is well known—have less than 600 amino acids in their major functional segment and share an identical triplet of leucine, glutamate, glutamate (LEE) at positions 342-344, and a phenylalaine (F) at position 422 when the last lysine (K) in the end of the sequence is counted as position 588. To clarify our invention, we have amended independent claims 9, 29 and 39 to affirmatively recite that the DNA polymerase in its unmodified state has leucine, glutamate, and glutamate residues at positions 342-344, respectively, and a phenylalanine at position 422, the positions being determined based on a last lysine residue in the end of the sequence counted as position 588. This, coupled with the recitation of the exact residue modifications (threonine, proline and leucine residues at positions 342-344, respectively, and a tyrosine residue at position 422), is believed to make the claims quite clear in the intent and scope of this invention.

In addition, we have amended claim 9 as suggested by the Examiner to read that the modified DNA polymerase has a reduction in the selective discrimination against the incorporation of fluorescent dye-labeled dideoxynucleotide terminators ddCTP and ddATP. Withdrawal of this rejection is believed to be in order.

Claims 9, 10, 13, 29, 30 and 39 were rejected under 35 U.S.C. §112, first paragraph. Separately, claims 9, 10 and 13 are further rejected under 35 U.S.C. §112, first paragraph. While we strongly disagree with the Examiner that the specification only enables claims limited to SEQ ID NO:4, in the interest of advancing allowance of this application we have amended the independent claims to specify that the DNA polymerase has an amino acid sequence that shares not less than 95% homology to SEQ ID NO:4. This, we

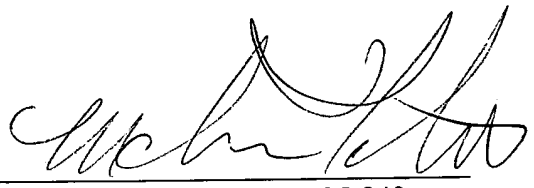
believe, should address the Examiner's concerns as stated, and withdrawal of these rejections are thought to be in order.

In the Office Action, the Examiner noted that the listing of references in the specification is not a proper information disclosure statement. These references were listed on a PTO-1449 form which was submitted with this divisional application when the divisional application was filed on February 2, 2000. Another copy of that PTO-1449 form is attached here for the Examiner's review.

Lastly, we note that the February 11, 2003 Office Action was mailed to the wrong address, to the attorneys who were previously of record in this case. To address this, we append here a copy of the signed power of attorney for the undersigned, which specifies the correct address. In addition, we also include a change of correspondence address. We request that all future mailings for this application be sent to the undersigned at Nash & Titus, LLC, at the correct address.

In summary, all of the Examiner's outstanding rejections and objections have been addressed, and the application is believed to be in allowable form. Notice to that effect is earnestly solicited. No amendment made was related to the statutory requirements of patentability unless expressly stated herein, and no amendment made was for the purpose of narrowing the scope of any claim unless we argued above that such amendment was made to distinguish over a particular reference or combination of references.

If the Examiner has any questions or would like to make suggestions as to claim language, he is encouraged to contact Marlana K. Titus at (301) 762-8214.

By: 

Marlana Titus, Reg. No. 35,843
Tel. No. (301) 762-8214

Nash & Titus, LLC
3415 Brookeville Road, Suite 1000
Brookeville, Maryland 20833

MARKED-UP VERSION OF ABOVE AMENDMENTS

IN THE SPECIFICATION:

On page 1, lines 1-6, first paragraph on the page, please amend as follows:

This application is a divisional application of Serial No. 09/157,397 (now U.S. Patent 6,165,765), filed September 21, 1998, which is a continuation-in-part application of Serial No. 08/544,643 (now U.S. Patent 5,747,298), filed October 18, 1995, and 08/642,684 (now U.S. Patent 5,834,253), filed May 3, 1996, and the entire contents of both applications are incorporated herein by reference.

IN THE CLAIMS:

Please amend claims 9, 29, 39 and 40 as follows.

9. (Amended) A host cell which produces a modified DNA polymerase having an amino acid sequence that shares not less than 95% homology to SEQ ID NO:4, which DNA polymerase during DNA sequencing effectively incorporated fluorescent dye-labeled dideoxynucleotide terminators ddCTP, ddATP, ddTTP and ddGTP, and [reduces] has a reduction in the selective discrimination against incorporation of fluorescent dye-labeled dideoxynucleotide terminators ddCTP and ddATP,

wherein the DNA polymerase in its unmodified state has leucine, glutamate, and glutamate residues at positions 342-344, respectively, and a phenylalanine at position 422, the positions being determined based on a last lysine residue in the end of the sequence counted as position 588, wherein the DNA polymerase selectively discriminates against incorporation of fluorescent dye-labeled dideoxynucleotide terminators ddCTP and ddATP but does not discriminate against incorporation of fluroescent dye-labeled dideoxynucleotide terminators ddTTP and ddGTP.

30. (Amended) A DNA construct comprising:

(iii) a nucleotide sequence encoding a modified DNA polymerase which has an amino acid sequence that shares not less than 95% homology [of] to a DNA polymerase isolated from a strain of *Bacillus stearothermophilus* of *Bacillus caldotenax*, having an amino acid sequence that shares not less than 95% homology to SEQ ID NO:4, which nucleotide sequence encodes threonine, proline and leucine residues at positions 342-344, respectively, and a tyrosine residue at position 422, wherein the DNA polymerase in its unmodified state has leucine, glutamate, and glutamate residues at positions 342-344, respectively, and a phenylalanine at position 422, the positions being determined based on a last lysine residue in the end of the sequence counted as position 588; and

(iv) a vector, for introducing the DNA construct into [euaryotic] eukaryotic and procaryotic host cells.

39. (Amended) A modified nucleotide sequence encoding a DNA polymerase which has an amino acid sequence that shares not less than 95% homology [of] to a DNA polymerase isolated from a strain of *Bacillus stearothermophilus* of *Bacillus caldotenax*, having an amino acid sequence that shares not less than 95% homology to SEQ ID NO:4, which nucleotide sequence encodes threonine, proline and leucine residues at positions 342-344, respectively, and a tyrosine residue at position 422, wherein the DNA polymerase in its unmodified state has leucine, glutamate, and glutamate residues at positions 342-344, respectively, and a phenylalanine at position 422, the positions being determined based on a last lysine residue in the end of the sequence counted as position 588.

40. (Amended) The modified nucleotide sequence according to claim 39 which has the nucleotide sequence of [SEQ ID:NO 3] SEQ ID NO:3.